## BRSK1 is required for myogenic differentiation of muscle precursor cells

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AMP-activated protein kinase (AMPK) and its related kinase (salt-inducible kinase)1 SIK1 have been reported to regulate myogenesis. Brain specific kinase 1 (BRSK1) is an AMPK-related kinase activated by LKB1 via Thr189 phosphorylation and is required for neuronal polarization in mammals. Three BRSK1 isoforms have been reported in the brain (long form, short form, S1 form), whereas there have been no studies of BRSK1 on myogenesis. We used C2C12 and L6 muscle precursor cells to study the role of BRSK1 in myogenic differentiation. Of the three BRSK1 isoforms, mRNA and protein analyses showed that C2C12 and L6 cells abundantly express the short form. Short form BRSK1 expression was increased during differentiation of C2C12 and L6 cells from myoblasts to myotubes. To study the function of short form BRSK1, wild type and mutant (Thr189Ala) BRSK1 were over-expressed in muscle precursor cells and shRNA was used to knock down BRSK1 (58%). Wild type BRSK1 over-expression had no effect on the proliferation and myogenic differentiation of L6 cells. BRSK1 knockdown inhibited myogenic differentiation, but had no effects on proliferation. Real-time PCR showed that myogenic regulatory factors MyoD and Myogenin were decreased after BRSK1 knockdown and remained lower after myogenic differentiation. Muscle specific genes Myosin Heavy Chain (MHC) and Glut4 were also down-regulated in knockdown cells. In summary, short form BRSK1 is expressed in C2C12 and L6 cells, and is induced during myogenic differentiation. Whereas BRSK1 over-expression does not further promote myogenic differentiation, knockdown of BRSK1 inhibits myogenic differentiation of muscle precursor cells. In addition, knockdown of BRSK1 results in lower expression of myogenic regulatory factors MyoD and Myogenin, as well as muscle specific genes MHC and Glut4. Future studies are needed to further investigate the underlying mechanisms.